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Use of Hypnosis in Studies of the Effect of Stress on Cardiovascular Function and Hormones

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ABSTRACT. In an attempt to separate the somatic and mental components of stress, groups of young male volunteers underwent running exercises and sauna baths, and roughly one year later had the same experiences recalled under hypnosis. In addition, experiments involving mental stress in the form of mental arithmetic were performed. A variety of physiological and biochemical parameters was measured on each occasion.

Results for cardiovascular responses, renin-angiotensin-aldosterone, cortisol, testosterone, androstenedione, prolactin and growth hormone are reported. It is concluded that the mental component of combined mental and somatic stress may be separated from the somatic component by hypnotic suggestion. The response during hypnotic suggestion of the stress is usually of less but sometimes of the same magnitude as that obtained during the actual stress. Occasionally the response goes in the opposite direction during hypnotic suggestion as compared to the real situation. The individual responses vary considerably between individuals. The hormones most sensitive to mental stress are growth hormone, androstenedione, cortisol, renin and angiotensin II. In the present study, mental stress had a depressing effect, if any, on plasma prolactin. Hypnosis in itself has no effect on plasma hormones in unstressed subjects compared to the normal diurnal variations.

Key words: hypnosis, heat stress, mental stress, physical exercise, renin, angiotensin, aldosterone, testosterone, androstenedione, cortisol, growth hormone, prolactin, blood pressure, heart rate

During studies on the effect of physical exercise and heat stress on cardiovascular function and various plasma hormones (1, 2, 3, 7, 11, 12, 15) it was realized that the responses measured were due to a combined effect of the somatic and mental components of the stress. It was therefore found necessary to find an experimental model which could give separate information on the two components. For this purpose hypnosis was chosen, because during hypnotic suggestion it is possible to reconstruct exactly the situation in previously performed actual stress experiments.

The present report gives a brief summary of results obtained with regard to cardiovascular function, the renin-angiotensin-aldosterone (RAA) system and some hormones in various experiments involving stress, compared to those obtained during hypnotic suggestion of the same stress. A few mainly preliminary results have previously been published (4, 14, 16, 22).

Abbreviations: RAA = renin-angiotensin-aldosterone, PRA = plasma renin activity, hGH = human growth hormone

METHODS

Three types of experiments were performed: —

1. Five male runners, 21—23 years old, ran 300 m at their maximum speed, three times, resting for 5 min between the first and second, and 3 min between the second and third runs. At the end of the third run all athletes were completely exhausted. Venous blood samples were taken before the warm-up period of 15 min, immediately (less than 30 sec) after the running exercise and several times after the test. All details, including results of biochemical parameters in blood and muscle tissue biopsies have been published previously (11, 11, 15, 17, 23). About 1 year later, at the same time of the day, hypnosis was induced by a common relaxing method using head-phones. By means of hypnotic suggestions, 4 of the athletes were returned to the scene (including the same weather conditions), events and mood of the actual running exercise that they performed earlier. All time periods were exactly the same. During the hypnotic »run» the test subjects lay still, without any noticeable movements of the limbs. However, the subjects hyperventilated during the last part of each »run» but were breathing normally during the »run» intervals. Blood samples were drawn at the same times as during the actual run and, in addition, before initiation of the hypnosis and before the »warming up» periods. Other experimental details have been published previously (14, 17, 23).

2. Eleven young male subjects were submitted to heat stress in a Finnish sauna (test sauna at the Finnish Sauna Society in Helsinki). The temperature of the sauna was 85—90°C and the absolute moisture content of the ambient air 46—47 g/kg. The participants stayed in the sauna for 20 min. Samples of venous blood were taken and pulse and arterial blood pressure measurements were made just before going into the sauna, after 10 min (6 subjects) and 20 min in the hot air, and 15 min (5 subjects), 30 min, 1 hour (5 subjects), 2 hours and 4—6 hours after the experiment. Further details of the experiment involving 6 of the subjects and the sampling procedures were described previously (3, 12). The sauna experiment was carried out on 2 separate occasions with 6 subjects in the first experiment and 5 in the second. In the experiments involving hypnosis, 9 of the 11 subjects participated. They were divided into 2 groups of 4 and 5 subjects, respectively. The hypnotic suggestion of sauna was given as described for the running experiment. The blood samples were taken about 20—30 min before the hypnotic suggestion of sauna, just before start of the »sauna» and after 10 min (4 subjects) and 20 min in the »sauna». The last samples were obtained at 1.5 hour after the »sauna», 30 min after finishing the hypnosis.

3. Six young male subjects volunteered for the mental stress study. They were asked to relax, especially during the last 30 min before the experiment. Exercises in mental arithmetic were carried out for 20 min between 11.00 and 12.00 hours in a quiet room with a temperature of about 20°C. The time of the day was the same as in the other two experiments. The mental arithmetic consisted of multiplication, division, addition and subtraction of whole numbers. A large number of problems were presented and the test subjects were asked to complete with each other in solving as many problems as possible in 20 min. Other details of this experiment have been described previously (13).

All assays were made in duplicates in most instances using radioimmunological methods, described in the previously cited reports. The matched pair t-test was used for statistical evaluation of the results.

RESULTS

Cardiovascular function

During the running exercise no measurements of blood pressure or pulse rate were made, but it is well established that pulse rate and systolic blood pressure increase and diastolic blood pressure decreases during running exercises. Immediately after the hypnotic »run», the systolic blood pressure of the subjects was slightly (8.7 %) but significantly increased as compared to the values before »warming-up». Simultaneously, the diastolic blood pressure decreased by 12.1 %. This decrease was already initiated during the »warming-up» period. The pulse rate increased by 37.9 % and all values returned to the »preexercise» level 30 min after the »run» (11). Thus, the response of the cardiovascular system during the hypnotic suggestion of running was weaker but in the same direction as the response during the actual exercise.

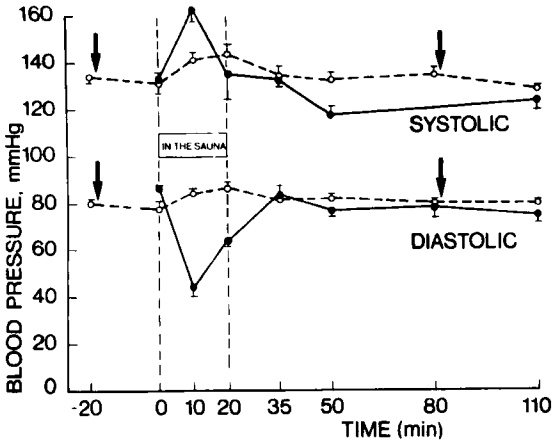

Fig. 1. Mean (± S.E.) of systolic and diastolic blood pressure in 9 young male subjects before, during and after heat stress in sauna (filled circles) and during hypnotic suggestion of sauna (open circles). The arrows indicate the start and end of hypnosis.

The response of the cardiovascular system to heat stress has been previously described for 6 subjects (12). In Fig. 1 the results for 9 subjects, both during actual heat stress in the sauna and during hypnotic suggestion of sauna are demonstrated. As found previously, the systolic blood pressure shows a rapid increase, followed after 20 min in the sauna by a decrease to the level experienced before the sauna. A further decrease to a minimum level occurs 30 min after the sauna. During hypnotic suggestion of sauna the systolic blood pressure increased slightly but significantly ($p < 0.001$) and was highest at the end of the »sauna» period. It returned within 15 min to the control level and no further decrease was observed, as after actual sauna. The diastolic blood pressure decreased rapidly during the first 10 min in the real sauna ($p < 0.005$) and partly returned to the pre-sauna level at the end of the sauna period (Fig. 1). The mean pre-sauna level was reached 15 min after the end of the sauna. During hypnotic suggestion of sauna the diastolic blood pressure increased slightly (10.5 %) but significantly ($p < 0.025$). The heart rate (Fig. 2) increased very rapidly during the intense heat stress and was highest 10 min after the start of the sauna period. It decreased to the control level 30 min after the sauna. The response during hypnotic suggestion of sauna was smaller and the highest rate was observed after 20 min in the »sauna». The »pre-sauna» level was obtained 15 min after the end of the »sauna» period.

The changes in blood pressure and heart rate during mental stress in the form of mental arithmetic have been previously described (13). The degree and direction of the changes are very similar to those found during hypnotic suggestion of sauna, but interestingly, after mental stress it took longer for the systolic blood pressure and heart rate to return to control levels. Since, in the actual sauna, the blood pressure changes are partly opposite to those obtained during hypnotic suggestion of sauna, it is likely that the perception of the hot environment during the actual sauna causes responses in the cardiovascular system partly counteracting the effect of the actual heat stress. During hypnotic suggestion of running the diastolic blood pressure fell, showing that the mental preparation for runninig gives a different blood pressure response to that obtained during mental stress.

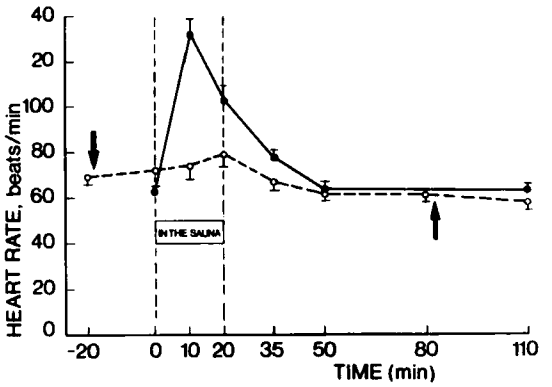

Fig. 2. Mean heart rate (± S.E.) in the same male subjects as in Fig. 1. Actual sauna bath = filled circles; hypnotic suggestion of sauna = open circles.

The renin-angiotensin-aldosterone (RAA) system

The results of the running experiments have been previously published (1, 11). They are summarized in Figs. 3—5. During actual running, the RAA system shows an intense activation with maximum blood levels of all components 30 min after the run. During hypnotic suggestion of running the changes are much smaller, but they are in the same direction, and maximum levels are obtained at the same time. For plasma renin activity (PRA) and angiotensin II, these changes are statistically significant. However, this was not so for aldosterone, because the level before the start of the hypnosis was rather high and did not decrease to the normal level of the participants before the hypnotic suggestion of competitive running was initiated. There was a tendency to a decrease in the mean level both of renin activity and angiotensin II during the first phase of hypnosis but the activation of the system seems to start already during the »warming-up» period, indicating that the participants were anticipating the competitive »run».

During heat stress there is a pronounced activation of the RAA system (3, 12) with a maximum level of plasma renin activity 15 min after sauna and of plasma aldosterone concentration 15—30 min after sauna. During hypnotic suggestion of the sauna a slight increase of PRA was noted during »sauna» with a maximum at the end of the »sauna» period ($p < 0.025$). For aldosterone, a slight increase was noted when comparing the end of the »sauna» period with 30 min after »sauna» ($p < 0.01$), which was probably due to the preceding increase of PRA.

The effect of mental stress in the form of mental arithmetic on the RAA system has been described and discussed in a previous communication (13). The increase of PRA was of the same magnitude as during the running exercise. However, angiotensin II increased

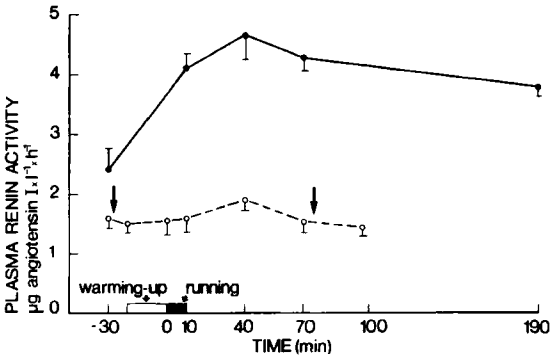

Fig. 3. Mean (± S.E.) plasma renin activity in 4 male athletes before, during and after exhaustive running exercise (filled circles) and during hypnotic suggestion of the same exercise (open circles). The arrows indicate the start and end of hypnosis.

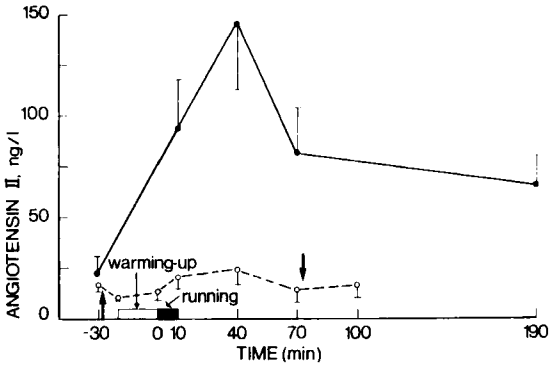

Fig. 4. Mean (± S.E.) of angiotensin II in the same male athletes as in Fig. 3. The arrows indicate the start and end of hypnosis.

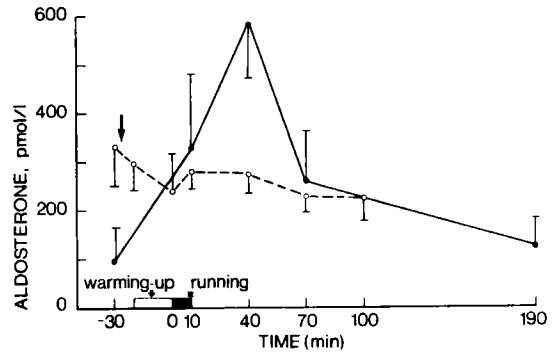

Fig. 5. Mean (± S.E.) of plasma aldosterone in the same male athletes as in Fig. 3. The arrows indicate the start and end of hypnosis.

much less and no significant increase in aldosterone was noted, perhaps due to high mean levels before the experiment. The peak levels of the different components of the RAA system were observed 15 min after finishing the mental arithmetic.

Other hormones

The alterations in the plasma level of cortisol, testosterone, androstenedione and growth hormone during the strenuous running experiment have been previously described (1, 15, 17). Mean plasma cortisol showed a tendency to increase after the run, but this was not statistically significant. During the hypnotic suggestion of running, the mean cortisol value increased slightly during the warming up period. This increase is probably due to anticipation of the competitive »run» and is a well-known phenomenon (9, 10, 19, 24). Because no sample was taken immediately before the run in the actual exercise experiment, this anticipatory increase could not be observed and a possible rise of plasma cortisol is hidden in the slight rise noted between the control and the value obtained after the run in some subjects.

There was a slight (13 %) but statistically significant ($p < 0.05$) increase of plasma testosterone at the end of the run and this was followed by a decrease below the basal level by about 25 % ($p < 0.05$). This was more than the normal decrease of testosterone (about 12 %) during the same period of the day in control experiments with the same subjects. During the hypnotic suggestion of running and in the mental stress experiment, only the normal diurnal variation of plasma testosterone could be noted.

Plasma androstenedione increased significantly during both the actual exercise (34 %; $p < 0.005$) and the mental suggestion of running (33 %; $p < 0.005$; Fig. 6). Thus, the response was identical in both experiments, demonstrating that the rise was due mainly if not exclusively to mental stress. A closer investigation of the results obtained during mental suggestion of running demonstrates that the main part of the increase occurred during the »warming-up» period which also indicates that the increase was mainly due to mental stress in the form of anticipation of the competitive »run». The decrease after the actual run was slower than after hypnotic suggestion of running (Fig. 6), which is most likely due to a decreased rate of metabolism of androstenedione in the liver after the exhaustive exercise.

For growth hormone (hGH), the responses during the actual strenuous running and during hypnotic suggestion of running were almost identical (Fig. 7). Because hGH is very sensitive even to slight stress, the basal levels were never »normal» during the days of the experiments. Therefore additional basal values were obtained from these subjects, and the means of 2—4 real basal values have been shown in Fig. 7. The individual variation in response was large as can be seen from the standard errors. In one subject, no response during the hypnotic suggestion of running could be observed. The increase in hGH seems mainly if not exclusively to be due to anticipation and perception of the competitive running exercise. At the time of these experiments, prolactin assays were unfortu-

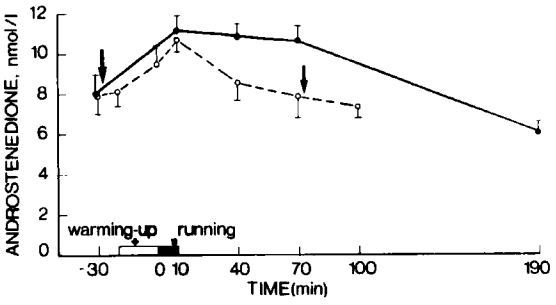

Fig. 6. Mean (± S.E.) of plasma androstenedione in the same male athletes as in Fig. 3. The arrows indicate the start and end of hypnosis.

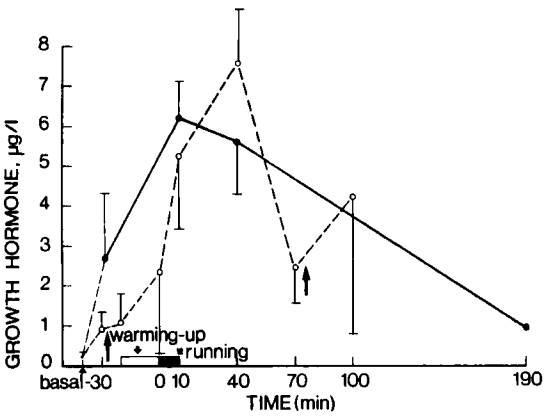

Fig. 7. Mean (± S.E.) of plasma growth hormone in the same male athletes as in Fig. 3. The arrows indicate the start and end of hypnosis.

nately not available, and no comparisons with the results obtained in the other experiments can be made.

The effect of heat stress in the sauna on the mean values of plasma cortisol, androstenedione, testosterone, growth hormone and prolactin are shown in Table I. The results for 6 individuals (4 included in this Table) have been previously published (2, 3). During, and especially after the sauna, plasma cortisol increased ($p < 0.005$). This was solely due to somatic stress caused by the heat, because during the hypnotic suggestion of sauna only the normal diurnal decrease of cortisol could be observed (Table 1). Androstenedione increased significantly 20—50 min after initiation of the sauna, with maximum levels at different times for different subjects. The mean increase was 76 % ($p < 0.0005$). There was also a slight increase of androstenedione during the same time period in the experiment with hypnotic suggestion of sauna, with the maximum values similarly at different times for different subjects. The increase was only 25 % ($p < 0.05$) but continued until the end of the hypnosis. The increase is even more significant because normally the androstenedione level decreases during the day.

The results for testosterone are very similar to those for androstenedione, except that there was no significant increase of plasma testosterone during sauna, but a significant decrease 30 min after sauna (14.4 %; $p < 0.01$). The hynotic suggestion of sauna caused a

Table I. *Effect of heat stress (20 min in Finnish sauna) and hypnotic suggestion of sauna on plasma cortisol (C; µmol/l) androstenedione (A; nmol/l), testosterone (T; nmol/l), growth hormone (hGH; µg/l) and prolactin (Prl; mIU/l) in 9 male subjects (mean values)*

Time in relation to sauna	n^a	Actual sauna					n^a	Hypnotic suggestion of sauna					
		C	A	T	hGH	Prl		C	A	T	hGH	Prl	
20 min before							9	0.32	4.1	24.8	0.9	199	
Immediately before	9	0.30	6.0	31.2	2.4	216	9	0.33	4.2	23.0	1.9	182	Hypnosis
10 min in	4	0.36	10.2	34.1	4.5	760	4	0.32	—	—	3.0	219	
20 min in	9	0.37	9.4	30.8	10.0	3102	9	0.29	4.3	25.3	4.5	172	
15 min after	5	0.57	7.9	30.8	13.2	—	9	0.28	4.3	24.9	5.3	179	
30 min after	9	0.68	9.3	26.7	9.9	2669	9	0.28	4.4	24.5	5.8	164	
60 min after	5	0.53	5.8	26.0	4.8	759	9	0.25	5.2	25.6	4.4	170	
90 min after							9	0.28	4.8	27.8	2.2	132	
120 min after	9	0.40	6.2	28.8	0.8	278							

[a] Number of subjects from whom samples were obtained and analyzed and used for calculation of mean values

slight but significant increase ($p < 0.01$) of plasma testosterone which continued to the end of the hypnosis, rather than the normal diurnal decrease. We believe that the increases of androstenedione and testosterone after the hypnotic suggestion of sauna are due to the feeling of well-being which normally occurs after sauna and which was suggested during hypnosis. It is not known why the pre-sauna levels of the androgens were higher before the real sauna as compared to the situation before the »sauna» after hypnotic suggestion. However, the real sauna experiments were carried out 2 months and 3 years, respectively, before the hypnotic suggestion of sauna and changes in basal levels of the steroids may have occurred with time.

Growth hormone increased significantly, both during and after the actual sauna ($p < 0.0025$) and to a lesser degree during and after the hypnotic suggestion of sauna ($p < 0.05$; Table I). The individual variation was very large. Some subjects did not react at all during the hypnotic suggestion of sauna, but during the actual sauna all responded with increased hGH levels. There was a huge increase of plasma prolactin (Fig. 8) during and after sauna, but the individual responses varied enormously. The smallest increase was 124 mIU/l and the largest 14177 mIU/l. During the hypnotic suggestion of sauna only the normal slight decrease was noted. Thus, the effect of sauna on plasma prolactin is solely due to the effect of the somatic stress in the form of heat. It should be mentioned that the hypnotic suggestion of heat was so strong that some individuals perspired during hypnosis.

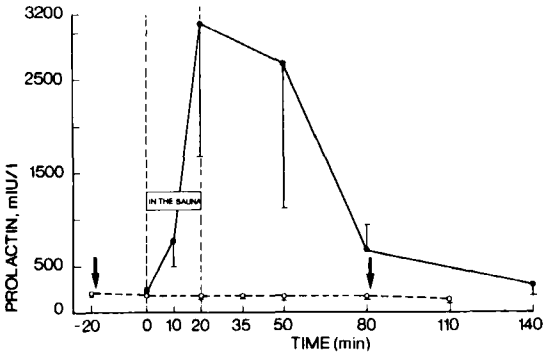

Fig. 8. Mean (± S.E.) of plasma prolactin in 9 young male subjects before, during and after sauna bath (filled circles) and during hypnotic suggestion of sauna (open circles). The arrows indicate the start and end of hypnosis.

Except for the normal diurnal decrease, no changes in plasma testosterone during mental stress in the form of mental arithmetic occurred. The other results are shown in Fig. 9. Because one of the 6 participants had a rather high level of cortisol before the experiment which then decreased, the increase in the mean value during and after the mental stress only approached statistical significance ($p < 0.1$). Androstenedione showed an 18.3 % increase ($p < 0.05$) and hGH a mean increase of 69.5 % ($p < 0.05$) but the individual variation was great and in two of the 6 subjects no hGH response at all was noted. Mental stress caused a statistically significant but slight decrease ($p < 0.05$) in plasma prolactin. Thus, mental stress seems not to influence prolactin secretion or perhaps may even cause a decrease which coincides with the highest mean increase of hGH. Because dopamine stimulates hGH release (5, 18) and inhibits prolactin release, dopaminergic stimulation would give the above-mentioned result (see also 25).

DISCUSSION AND CONCLUSIONS

Only the effect of physical exercise on plasma hormones (1, 7, 11, 15, 17) and of hypnotic suggestion of running (14), heat stress (12) and mental stress in the form of mental arithmetic (13) on the RAA system have been previously discussed in detail. Because of the large number of results and the fact that other hormones, not mentioned here, were also

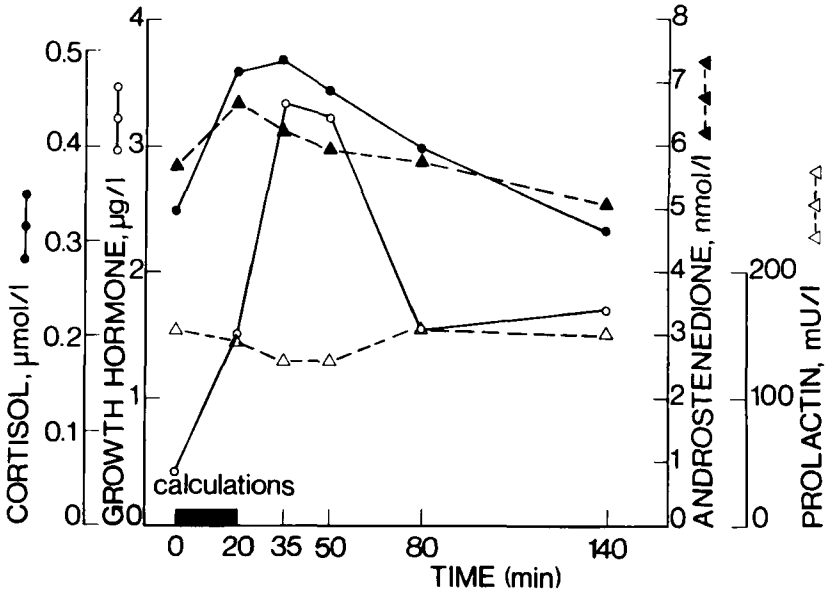

Fig. 9. Mean plasma cortisol, growth hormone, androstenedione and prolactin in 6 young male subjects before, during and after mental stress in the form of mental arithmetic.

measured, this work will be presented in more detail elsewhere. We will limit this discussion to some specific points of interest.

Most of the responses to stress measured in these experiments are the result of increased sympathetic activity and increased secretion of adrenaline and noradrenaline from the adrenal medulla. More intense stress additionally activates the hypothalamo-hypophyseo-adrenal axis. Not only the intensity seems to be important, but also the nature of the stress. For example, in squirrel monkeys (6) it was possible to produce separate effects on growth hormone and cortisol level or on both together depending on the nature of the stress. The nature of the response may also depend on the coping behaviour of the individuals (8). In addition, there are extremely large individual variations in the magnitude of the response (see also 21), which also could be observed in the present study. For example, the increase of growth hormone after the different kinds of stress varied between individuals from zero to 500—1000 % above the basal level. Heat stress in the sauna in some individuals caused 30-fold increases of prolactin and in others only 2-3-fold increases. These large differences in individual response may partly explain the differences in results obtained for prolactin levels in heat stress (20). Our experiments clearly show that the mental component of heat stress in the sauna does not influence plasma prolactin levels at all, and also that mental stress in the form of mental arithmetic does not change the prolactin level or may even slightly decrease it.

The observation that the increase of androstenedione and hGH during short-term physical competitive exercise is of the same magnitude as that induced by hypnotic suggestion of the same type of competitive running is interesting. There was a tendency to an elevation of plasma cortisol during the actual running, but during hypnotic suggestion of running no such increase was observed. Thus, in the latter situation andros-

tenedione increased significantly without any concomitant increase of cortisol, suggesting that androstenedione production may be stimulated by means other than ACTH. Because the subjects were laying on a bed, changes in the metabolism of androstenedione could hardly have caused the increased levels. The decrease of androstenedione is more rapid than that of cortisol after heat and mental stress and this delay in the elimination of cortisol as compared to androstenedione could be a result of their different metabolism.

Control experiments with hypnosis without any suggestion of stress demonstrated similar behaviour of plasma hormone levels as obtained in non-hypnotized resting subjects. If the subjects were excited before the experiment, hypnosis regularly caused a decrease of the plasma level of those hormones reacting most sensitively to mental stress.

The sauna bath seems generally not to cause any mental stress, as judged from the results of the hormone analyses during the hypnotic suggestion af sauna. This is in accordance with the general view that the sauna bath is mentally relaxing. Because of the rather long stay in the sauna (exceeding the normal time), some stress was obviously experienced by two or three sensitive individuals and this could be observed during the hypnosis. The high temperature of the actual sauna, however, causes a number of hormonal alterations similar to those observed in long-distance running (7).

The main general conclusions to be drawn are as follows: —

1. The mental component of combined mental and somatic stress may be separated from the somatic component by hypnotic suggestion.

2. The quality and quantity of the cardiovascular and hormonal response to mental and somatic stress varies considerably from one individual to another.

3. The hormonal response during hypnosis is essentially related to that observed during the actual stress experiment, but sometimes it is in the opposite direction. In combined stress, a hormone response may be exclusively due either to the somatic or the mental component of the stress, or to both.

4. The most sensitive hormone to mental stress is growth hormone. However, some very calm subjects do not react at all, and thus the between-individual variation is great.

5. Other hormones reacting to mental stress are renin, angiotensin II, cortisol and androstenedione. In our experiments, mental stress had a depressing effect, if any, on the plasma prolactin.

6. Hypnosis in itself has a depressing, if any, effect on stress hormone levels, blood pressure and heart rate, because external stress factors are eliminated. In subjects with basal pre-hypnosis hormone levels, no effect except for normal diurnal variation patterns can be observed. It should be pointed out that during hypnosis the subjects do not show any changes in their plasma hormone levels which would parallel those observed during normal sleep. The levels are identical with those obtained during normal rest at the same actual time of the day.

7. Significant changes of pulse rate and blood pressure can be induced during hypnotic suggestion of running and sauna bath. These alterations are probably caused by high motivation during the competitive »run» and the experience of the »hot environment» during hypnosis.

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DISCUSSION

Dr R. L. Verrier (Boston) wondered whether any evidence of cardiovascular conditioning was found as a result of exposure to the sauna.

Professor Adlercreutz said that both the cardiovascular and the hormonal systems underwent changes in the sauna similar to those seen during long distance running. In a sense, therefore, Finnish sportsmen also trained in the sauna. He did not know of any investigation to establish whether regular attendance at the sauna increased fitness, but such a study would be interesting. There were, however, many studies of the possible adverse effects of the sauna and the general conclusion was that it did not produce a higher frequency of arrhythmias or any adverse changes.

Dr M. Partinen (Helsinki) said that they had found a peak in growth hormone during the deep slow wave period of sleep. They considered this to be a recuperative anabolic state but a similar increase was apparently observed during physical exercise.

Professor Adlercreutz said that if the growth hormone peak were measured throughout the night it was found to be smaller in the well trained than the poorly trained individual. In a sense, this was a way of investigating fitness levels. The unfit had high levels of activity, because they required a greater anabolic effect than did fit individuals in order to prepare for the following day.

Dr D. W. Johnston (Oxford) asked whether individuals who were hypnotised to imagine that they were running actually started to tense their muscles.

Professor Adlercreutz said that no visible movements of the muscles could be observed. However, in the last third of hypnotised »running» they actually showed hyperventilation.

Dr S. Chierchia (London) wondered whether the effects of hyperventilation without hypnotism had been investigated. Decreasing the pH could produce very marked changes in the availability of calcium ions in nervous tissue.

Professor Adlercreutz said that this might well be done as a control experiment. However, the hyperventilation effect itself was seen only in the final stages of the hypnotised »run».

When asked why volunteers had prolonged the sauna visit to 20 min, he said that they had been interested in the effect of increased temperature stress. There was evidence from marathon runners that the hormonal effect was largely dependent on the body temperature. He had therefore wished to investigate this temperature effect more fully. Temperature produced high levels of somatic, though usually not of mental, stress.